IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Haberbosch, et al.
Serial No.	:	10/655,225
Filed	:	September 4, 2003
For	:	3-DEAZAADENOSINE PREVENTS ATHEROSCLEROSIS AND GRAFT VASCULOPATHY
Art Unit	:	1615
Examiner	:	Carlos A. Azpuru

May 20, 2008

This is to certify that this correspondence is being sent electronically to: Commissioner for Patents, P. O. Box 1450, Alexandria, Va. 22313-1450 on the date shown below
.

James R. Crawford /jrc/ May 20, 2008

APPEAL BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

As required under 37 C.F.R. § 41.37(a), this brief is filed within two months of the Notice of Appeal filed in this case on March 20, 2008, and is in furtherance of said Notice of Appeal.

Please charge the required fees under 37 C.F.R. § 41.20(b)(2) to deposit account no. 50-0624.

This brief contains items under the following headings as required by 37 C.F.R. § 41.37 and M.P.E.P. § 1206:

I.	Real Party In Interest
II	Related Appeals and Interferences
III.	Status of Claims
IV.	Status of Amendments
V.	Summary of Claimed Subject Matter
VI.	Grounds of Rejection to be Reviewed on Appeal
VII.	Argument
VIII.	Claims Appendix
IX.	Evidence Appendix
X.	Related Proceedings Appendix

I. REAL PARTY IN INTEREST

The real party in interest for this appeal is the assignee, Kerckhoff-Klinik Gesellschaft Mit Beschrankter Haftung.

II. RELATED APPEALS, INTERFERENCES, AND JUDICIAL PROCEEDINGS

There are no other appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

A. Total Number of Claims in Application

There are 24 claims pending in this application.

B. Current Status of Claims

1. Claims canceled: 1-17 and 23-25
2. Claims pending: 18-22 and 26-44
3. Claims allowed: None
4. Claims rejected: 18-22 and 26-44

C. Claims On Appeal

The claims on appeal are all finally rejected claims, i.e., claims 18-22 and 26-44.

IV. STATUS OF AMENDMENTS

All amendments are believed to have been entered.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The invention relates generally to the use of 3-deazaadenosine or related salts, or analogs thereof which degrade to 3-deazaadenosine in a body, to prevent various vascular diseases or graft rejection. More specifically, the presently claimed subject matter relates to a stent coated with 3-deazaadenosine or an analog of 3-deazaadenosine selected from the group consisting of a salt of 3-deazaadenosine and a precursor of 3-deazaadenosine which degrades to 3-deazaadenosine in a body under physiological conditions (See, e.g., page 4, lines 30-33 to page 5, line 1 of the specification). Methods of treating method of treating in-stent restenosis, a reperfusion injury, an infectious coronary syndrome, an inflammatory coronary syndrome, dilated cardiomyopathy, viral myocarditis or a reperfusion injury by implanting a stent coated with 3-deazaadenosine or a related salt or analog into a patient in need thereof are also claimed (See, e.g., specification page 4, lines 25-32 to Page 5, lines 1-6).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Did the Examiner err by rejecting claims 18-22 and 26-44 under 35 U.S.C. §103(a) over US Patent No. 4,322,411 (Vinegar)in view of US 2003/0203976 ("Hunter") in view of U.S. Patent No. 5,234,456 ("Silvestrini")?

VII. ARGUMENT

The claims do not stand or fall together as will be apparent from the arguments which follow.

It should be noted that the Examiner applies a broad-brush general allegation against the presently pending claims and ha not addressed each and every feature of the claims as required in order to establish a prima facia case of obviousness. Specifically, the Examiner has not addressed to the following limitations of the claims, which are underlined:

Claim 18. A stent coated with 3-deazaadenosine or an analog of 3-deazaadenosine selected from the group consisting of a salt of 3-deazaadenosine and a precursor of 3-deazaadenosine which degrades to 3-deazaadenosine in a body under physiological conditions.

19. The stent of claim 18, wherein said analog of deazaadenosine is selected from the group consisting of 3-deazaadenosine-3'-monophosphoric acid, 3-deazaadenosine-3'5'-cyclophosphate and 3-deazaadenosine-5'-diphosphoric acid.

20. The stent of claim 18, wherein said 3-deazaadenosine or analog of 3-deazaadenosine is covalently bound to the stent.

21. A method of treating in-stent restenosis, a reperfusion injury, an infectious coronary syndrome, an inflammatory coronary syndrome, dilated cardiomyopathy, viral myocarditis or a reperfusion injury comprising implanting the stent of claim 18 in a patient in need thereof.

22. The method of claim 21, wherein in-stent restenosis is treated.

26. The stent of claim 18, wherein said analog of deazaadenosine is 3-deazaadenosine-3'-monophosphoric acid.

27. The stent of claim 18, wherein said analog of deazaadenosine is 3-deazaadenosine-3'5'-cyclophosphate.

28. The stent of claim 18, wherein said analog of deazaadenosine is 3-deazaadenosine-5'-diphosphoric acid.

29. The stent of claim 26, wherein said analog is covalently bound to the stent.

30. The stent of claim 27, wherein said analog is covalently bound to the stent.

31. The stent of claim 28, wherein said analog is covalently bound to the stent.

32. A method of treating reperfusion injuries comprising implanting the stent of claim 18 in a patient in need thereof.

33. A method of treating an infectious coronary syndrome comprising implanting the stent of claim 18 in a patient in need thereof.

34. A method of treating an infectious coronary syndrome comprising implanting the stent of claim 19 in a patient in need thereof.

35. A method of treating an inflammatory coronary syndrome comprising implanting the stent of claim 18 in a patient in need thereof.

36. A method of preventing an inflammatory coronary syndrome comprising implanting the stent of claim 18 in a patient in need thereof.

37 A method of treating dilated cardiomyopathy comprising implanting the stent of claim 18 in a patient in need thereof.

38. A method of treating dilated cardiomyopathy comprising implanting the stent of claim 19 in a patient in need thereof.

39. A method of treating viral myocarditis by implanting the stent of claim 18 in a patient in need thereof.

40. A method of treating viral myocarditis by implanting the stent of claim 19 in a patient in need thereof.

41. A method according to claim 21, wherein the method comprises treating in-stent restenosis, an inflammatory coronary syndrome, dilated cardiomyopathy, or viral myocarditis.

42. A method according to claim 21, wherein the method comprises treating in-stent restenosis, a reperfusion injury, an inflammatory coronary syndrome, or dilated cardiomyopathy.

43. The method of claim 41, wherein in-stent restonosis or viral myocarditis is treated.

44. The method of claim 42, wherein a reperfusion injury or an inflammatory coronary syndrome is treated.

Thus, it is difficult to address the Examiner's rejections because the rejection amounts to a mere general allegation of obviousness based on a combination of references. We recognize that "the [obviousness] analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ". With respect to an obviousness analysis, the U.S. Supreme Court requires that "[t]o facilitate review, this analysis should be made explicit." KSR Int'l v. Teleflex Inc., 127 S. Ct. 1727, 1741 (2007). As can be seen from the lack of discussion as to the specific features of claims underlined above, the Examiner did not make such an explicit analysis so the Section 103(a) rejection of claims must be withdrawn.

Furthermore, there is no specific teaching cited to by the Examiner disclosing the use of deazaadenosine to treat the claimed disease states or conditions, i.e., stent restenosis, a reperfusion injury, an infectious coronary syndrome, an inflammatory coronary syndrome, dilated cardiomyopathy, viral myocarditis, infectious coronary syndrome, or a reperfusion injury, set forth individually or in various combinations in method claims 21-22, and 32-44. In fact, none of these disease states were specifically addressed by the Examiner.

With respect to claims 18-20 and claims 26-31 the Examiner only suggests that 3-deazaadenosine is disclosed by Vinegar, but does not suggest that any other feature is specifically disclosed, e.g., a salt of 3-deazaadenosine or a precursor which degrades to 3-deazaadenosine in the body under physiological conditions such as set for the in claims 18-20 and 26-31.

More specifically, the active agents 3-deazaadenosine-3'-monophosphoric acid, 3-deazaadenosine-3'5'-cyclophosphate and 3-deazaadenosine-5'-diphosphoric acid are not discussed at all by the Examiner.

This rejection appears to be based on improper hindsight reasoning. For reasons set forth below, at the priority date of the invention, there was no reason for one skilled in the art to combine the cited references as proposed by the Examiner.

An advantage of a coated stent of the invention is the provision of a medical devise capable of delivering and eluting the active ingredient 3-deazaadenosine directly at the injured vascular site.

Vinegar discloses that 3-deazaadenosine is a potent anti-inflammatory agent and thus suitable for the treatment of inflammation. According to Vinegar, clinical conditions with which inflammation is associated include arthritis, rheumatoid arthritis and osteoarthritis, postoperative inflammation, dental inflammation, acute and chronic ocular inflammatory diseases, and conjunctivitis. In contrast, presently claimed invention relates to the treatment of in-stent restenosis, reperfusion injury, infectious or inflammatory coronary syndrome, dilated cardiomyopathy and viral myocarditis. The skilled artisan cannot ascertain from Vinegar that 3-deazaadenosine can be used for the treatment of the claimed diseases.

Furthermore, according to Vinegar, 3-deazaadenosine is orally, systemically and locally active. Vinegar, however, does not contain any teaching or suggestion to the particular application of the presently claimed invention, namely as a coating on a stent. If a skilled artisan even decided to use 3-deazaadenosine as anti-inflammatory agent in view of Vinegar, there was no motivation to use a method of administration not disclosed by Vinegar.

In sum, neither the suitability of 3-deazaadenosine for the treatment of the particular diseases of the invention nor the administration of 3-deazaadenosine as a coating on a stent is taught or suggested by Vinegar.

Silvestrini describes a stent for placement within a body lumen. Silvestrini focuses on the structure of the stent described therein, which is engineered such that the stent, when positioned and subsequently inflated, supports a lumen. A therapeutic drug can be included for release at the site of stent placement. As disclosed in column 3, lines 15-20, non-limiting examples of such drugs include, among others, anti-inflammatory drugs. Thus, inflammatory agents are just one possibility of many agents which are suitable in principle. However, Silvestrini does not appear to provide any specific examples of anti-inflammatories which can be used in combination with the disclosed stent.

Clearly Silvestrini does not address covalent binding of the active to the stent as required by claims 20, 29, 30 and 31.

Furthermore, Silvestrini only mentions the inclusion of anti-inflammatories for "suppression of biologic response to stenting or balloon angiography: (col. 3, lines 19-20). Silvestrini does not suggest using 3-deazaadenisone as a primary treating agent, only as an adjunct to reduce side effects of stent or angiography procedures.

Hunter discloses anti-angiogenic compositions and methods for the use thereof, and discloses stents which may be coated with an anti-angiogenic composition and which may additionally include other agents such as anti-inflammatories (Par. [0151]). Additionally, the anti-angiogenic composition may comprise a wide variety of compounds. Paragraph [0151] lists several kinds of active agents and names some representative examples of anti-inflammatory agents such as steroids and non-steroidal anti-inflammatory drugs. 3-deazaadenosine is not disclosed. Note that Vinegar teaches that 3-deazaadenosine is different from known anti-inflammatory agents (See col. 1, line 44 to col. 2, line 6) and may in fact be used with other anti-inflammatory agents. Thus, successful use of 3-deazaadenosine in a stent could not be predicted from the disclosure of the cited references. It is not alleged that Hunter would overcome any deficiencies described above

There is no disclosure in any of the cited references that 3-deazaadenosine shows any favorable effects when used as a coating on a stent. To Applicants knowledge, never before had anybody tried to determine whether this substance is at all suitable for this application form. Thus, if the skilled artisan would have decided to use an anti-inflammatory agent in combination with one of the stents of Hunter or Silvestrini, he would most likely selected a drug which is commonly used in combination with stents, and, not only that, he would not have selected the anti-inflammatory as a primary therapeutic agent since they both suggest the use of an anti-inflammatory as an adjunct to a primary therapeutic. Since Silvestrini and Hunter do not give much guidance on how to select the anti-inflammatory drug, and Vinegar describes 3-deazaadenosine as a non-traditional anti-inflammatory, the skilled person would have considered documents which describe active agents for a use as coating on a stent; however, it is respectfully submitted that he would not have considered 3-deazaadenosine in this context. Only someone aware of the teaching of the presently claimed invention would be guided to use 3-deazaadenosine, which clearly shows that the rejection is based on impermissible hindsight.

Additionally, the subject matter of claims directed to methods of treatment with the stent of the invention is not taught or suggested by the combination of Silvestrini, Hunter and Vinegar. The claimed methods of treatment are based on the mechanism by which 3-deazaadenosine exerts its favorable effect. The suitability for the treatment and prevention of restenosis is not only due to the anti-inflammatory action of this substance. In the past, no significant prevention of restenosis could be achieved. The inventors of the presently claimed invention were able to show for the first time that the application of 3-deazaadenosine significantly reduces restenosis.

Besides inflammatory responses, the proliferation of human coronary vascular smooth muscle cells (VSMC) comprises a major determinant in the development of atherosclerosis and restenosis. Current data show that in addition to its anti-inflammatory action, 3-deazaadenosine dose-dependently prevents the proliferation and migration of human coronary vascular smooth muscle cells (VSMC). To demonstrate this effect, attached is a recent scientific article of the inventors. It is only by exerting potent anti-proliferative and anti-inflammatory properties that 3-deazaadenosine provides an improved approach to

prevent vascular proliferative diseases, and this favorable effect was not known before the present invention.

The Supreme Court has said that, "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." KSR, 127 S.Ct at 1741. The Court further noted that "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." KSR, 127 S.Ct at 1741. Even assuming *arguendo* that all of the elements are disclosed in the cited references; the Examiner has not identified any reasonable reason to combine the reference as alleged.

"[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." In re Fritch, 972 F.2d 1260, 1265 (Fed. Cir. 1992) (citations omitted, bracketed material in original). Clearly, the Examiner has not met this burden.

In summary, the rejection of claims under 35 U.S.C. §103(a) should be withdrawn for at least the reasons set forth above.

VIII. CLAIMS APPENDIX

A copy of the claims involved in the present appeal is attached hereto as Appendix A.

IX. EVIDENCE APPENDIX

No evidence pursuant to §§ 1.130, 1.131, or 1.132 is being submitted.

X. RELATED PROCEEDINGS APPENDIX

No related proceedings are referenced in II. above, hence copies of decisions in related proceedings are not provided (see Appendix C).

A favorable decision is earnestly solicited.

Dated: May 20, 2008

Respectfully submitted,

By_____/jrc/_____
James R. Crawford
Registration No.: 39,155
FULBRIGHT & JAWORSKI L.L.P.
666 Fifth Avenue
New York, New York 10103
(212) 318-3148
(212) 318-3400 (Fax)
Attorney for Applicant

APPENDIX A

Claims 1-17 (canceled)

18. (previously presented) A stent coated with 3-deazaadenosine or an analog of 3-deazaadenosine selected from the group consisting of a salt of 3-deazaadenosine and a precursor of 3-deazaadenosine which degrades to 3-deazaadenosine in a body under physiological conditions.

19. (previously presented): The stent of claim 18, wherein said analog of deazaadenosine is selected from the group consisting of 3-deazaadenosine-3'-monophosphoric acid, 3-deazaadenosine-3'5'-cyclophosphate and 3-deazaadenosine-5'-diphosphoric acid.

20. (previously presented): The stent of claim 18, wherein said 3-deazaadenosine or analog of 3-deazaadenosine is covalently bound to the stent.

21. (previously presented) A method of treating in-stent restenosis, a reperfusion injury, an infectious coronary syndrome, an inflammatory coronary syndrome, dilated cardiomyopathy, viral myocarditis or a reperfusion injury comprising implanting the stent of claim 18 in a patient in need thereof.

22. (previously presented): The method of claim 21, wherein in-stent restenosis is treated.

Claims 23-25 (canceled)

26. (previously presented) The stent of claim 18, wherein said analog of deazaadenosine is 3-deazaadenosine-3'-monophosphoric acid.

27. (previously presented) The stent of claim 18, wherein said analog of deazaadenosine is 3-deazaadenosine-3'5'-cyclophosphate.

28. (previously presented): The stent of claim 18, wherein said analog of deazaadenosine is 3-deazaadenosine-5'-diphosphoric acid.

29. (previously presented) The stent of claim 26, wherein said analog is covalently bound to the stent.

30. (previously presented) The stent of claim 27, wherein said analog is covalently bound to the stent.

31. (previously presented) The stent of claim 28, wherein said analog is covalently bound to the stent.

32. (previously presented) A method of treating reperfusion injuries comprising implanting the stent of claim 18 in a patient in need thereof.

33. (previously presented) A method of treating an infectious coronary syndrome comprising implanting the stent of claim 18 in a patient in need thereof.

34. (previously presented) A method of treating an infectious coronary syndrome comprising implanting the stent of claim 19 in a patient in need thereof.

35. (previously presented) A method of treating an inflammatory coronary syndrome comprising implanting the stent of claim 18 in a patient in need thereof.

36. (previously presented) A method of preventing an inflammatory coronary syndrome comprising implanting the stent of claim 18 in a patient in need thereof.

37 (previously presented) A method of treating dilated cardiomyopathy comprising implanting the stent of claim 18 in a patient in need thereof.

38. (previously presented) A method of treating dilated cardiomyopathy comprising implanting the stent of claim 19 in a patient in need thereof.

39. (previously presented) A method of treating viral myocarditis by implanting the stent of claim 18 in a patient in need thereof.

40. (previously presented) A method of treating viral myocarditis by implanting the stent of claim 19 in a patient in need thereof.

41. (previously presented)A method according to claim 21, wherein the method comprises treating in-stent restenosis, an inflammatory coronary syndrome, dilated cardiomyopathy, or viral myocarditis.

42. (previously presented)A method according to claim 21, wherein the method comprises treating in-stent restenosis, a reperfusion injury, an inflammatory coronary syndrome, or dilated cardiomyopathy.

43. (previously presented)The method of claim 41, wherein in-stent restonosis or viral myocarditis is treated.

44. (previously presented)The method of claim 42, wherein a reperfusion injury or an inflammatory coronary syndrome is treated.

APPENDIX B

None

APPENDIX C

None